UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,125	06/13/2006	Per Holm	20481/0206897-US0	5556

7278 7590 05/25/2010

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
05/25/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,125	HOLM ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-23,36,39-41,43,45-51,53-57,59,66,71,73,75,77,80-82,84 and 86-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 2-23,36,39-41,43,45-51,53-57,59,66,71,73,75,77,80-82,84 and 86-90.

DETAILED ACTION

1. Applicants' arguments, filed March 15, 2010, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 2 – 23, 36, 39 – 41, 43, 45 – 51, 53 – 57, 59, 66, 71, 73, 75, 77, 80 -82, 84 and 86 – 90 were rejected under 35 U.S.C. 103(a) as being unpatentable over Holm et al. (WO 03/004001) in view of Yamashita et al. (US 6,576,259) and the Merck Index entry for tacrolimus. This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed December 15, 2009 and those set forth below.

Applicant traverses this rejection on the grounds that WO '001 does not disclose dispersing tacrolimus in a mixture of PEG and poloxamer or adding a release-rate modifier after the dispersion has been sprayed onto a second composition and the '259 patent teaches away from dispersion tacrolimus in a mixture of PEG and poloxamer as that document uses a solid base like HPMC to provide sustained release. These arguments are unpersuasive. While compositions of tacrolimus and HPMC with the PEG and poloxamer ingredients are not taught by Holm, those elements are taught by the secondary, Yamashita reference. "[T]he prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed…." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). **MPEP 2123**. Solidd rug containing particles are obtaining using different methodolodes

– the one of Holm closely mirrors that of the instant claims while the method of Yamashita is different but different ways of making the solid particles does not rise to the level of teaching away.

Applicant also argues that the Examiner has not provided any teaching or suggestion that the organic solvent method taught by '259 is compatible with the use of a PEG/poloxamer mixture. Neither reference discloses or suggests adding at the release rate modifier to the tacrolimus composition by dry mixing. These arguments are unpersuasive. The organic solvent method of Yamashita is not required as the organic solvent technique is used to produce solid particles containing drug in a sustained release matrix. The methodology of Holm using the PEG/poloxamer techniques taught therein also results in the production of solid particles containing drug in a sustained release matrix. Thus, it is not required that the organic solvent methodology be compatible with the PEG/poloxamer solution as solid particles containing drug in a sustained release matrix are produced. Yamashita describes additional processing of the solid particles containing drug in a sustained release matrix by the additional of excipients that include HPMC, a release rate modifier. Holm also states that drug/PEG/poloxamer particulate material can be further used to manufacture dosage forms (p 27 ln 20 onward) and HPMC as a filler, diluent and/or binder (p 21, ln 22 – p 22, ln 2). Dry granulation, a common technique known to those of ordinary skill in the pharmaceutical formulation art and mentioned by Holm et al., is dry mixing process. The cited prior art and the knowledge of one ordinary skill in the art renders obvious the instant method and compositions produced by that process. Applicants have not shown

secondary consideration such as unexpected properties that result from dry mixing as opposed to other methods such as wet granulation that could overcome the *prima facie* case of obviousness.

Applicant also argues that the Examiner has not provided any rational as to why the ordinary skilled artisan would have selectively picked a particular substances from WO '001 as a vehicle for tacrolimus instead of the ethanol and HPMC taught in the '259 Patent. This argument is unpersuasive. The sentence bridging p 8 – 9 and the beginning of the next paragraph in the December 15, 2009 Office Action provides that rationale. The PEG 6000/poloxamer 188 mixture from Holm increases bioavailability of active agents with very low aqueous solubilities and tacrolimus is one such agent. Yamashita provides information on the desired sustained release profile of the tacrolimus when administered that can be achieved through the use of HPMC as material that alters the release profile. The resulting dosage form will have delayed release and higher bioavailability.

Based on the above arguments, Applicants state that it appears that the Examiner is using impermissible hindsight reasoning. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d

1392, 170 USPQ 209 (CCPA 1971). The reasoning used is discussed in greater detail in the paragraphs above.

Lastly, Applicants argue that claims 83 - 85 and 90 are product-by-process claims. [Claims 66, 84 and 90 are the pending product-by-process claims.] The compositions of the cited prior art are made by a different process with different components that are necessarily structurally different from the presently claimed compositions. These arguments are unpersuasive. As discussed in the greater detail above, compositions with the required ingredients are taught by the cited prior art and the method by which those composition is prepared is obvious over the cited prior art.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

NMW